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## Ischaemic heart disease

### Troponins to guide the use of invasive treatment in ACS ►

Comparing conservative to invasive treatment in patients with acute coronary syndromes (ACS) treated with tirofiban, early invasive treatment showed an 18% reduction in death/myocardial infarction (MI)/repeat ACS within six months. A total of 2220 patients with ACS were enrolled and 1780 completed the six month follow up with cardiac troponin-I (cTnI) available. Patients with a cTnI concentration of  $> 0.1$  ng/ml experienced a significant reduction in the primary end point with the invasive versus conservative strategy (15.3% v 25.0%; odds ratio (OR) 0.54, 95% confidence interval (CI) 0.40 to 0.73). Patients with cTnI concentrations of  $< 0.1$  ng/ml had no benefit from early invasive management (16.0% v 12.4%; OR 1.4, 95% CI 0.89 to 2.05,  $p < 0.001$  for interaction). Similar results were observed with cTnT.

▲ **Morrow DA**, Cannon CP, Rifai N, Frey MJ, Vicari R, Lakkis N, Robertson DH, Hille DA, DeLuca PT, DiBattiste PM, Demopoulos LA, Weintraub WS, Braunwald E, for the TACTICS-TIMI 18 Investigators. Ability of minor elevations of troponins I and T to predict benefit from an early invasive strategy in patients with unstable angina and non-ST elevation myocardial infarction: results from a randomized trial. *JAMA* 2001;**286**:2405–12.

### Why blood pressure falls on cardiopulmonary bypass ►

Hypotension caused by a reduction in systemic vascular resistance (SVR) is a recognised complication of cardiopulmonary bypass (CPB), and may necessitate the administration of inotropic drugs. This has traditionally been attributed to a generalised inflammatory response in the extracorporeal circulation. Bradykinin, a potent vasodilator that also increases vascular permeability, may accumulate during cardiopulmonary bypass due to the exclusion of the lungs from the circulation where bradykinin is degraded by angiotensin converting enzyme (ACE), and may thus contribute to the drop in SVR. In 27 patients undergoing CPB for cardiac surgery, plasma bradykinin concentrations increased progressively during cardiopulmonary surgery, and were increased four-fold by the end of cardiopulmonary bypass. Plasma bradykinin concentrations were inversely correlated with mean arterial pressure, which fell progressively until the end of surgery (–18 mm Hg), and were also inversely correlated with SVR. Bradykinin concentrations fell by 60% when the pulmonary circulation was fully restored, while the patients were still receiving CPB. Longer cardiopulmonary weaning times and the recently developed bradykinin receptor antagonists may help prevent the reduction in SVR during CPB.

▲ **Cugno M**, Nussberger J, Biglioli P, Alamanni F, Coppola R, Agostoni A. Increase of bradykinin in plasma of patients undergoing cardiopulmonary bypass: the importance of lung exclusion. *Chest* 2001;**120**:1776–82.

**The pill does increase MI risk ►** The possible association between the use of oral contraceptives and the risk of MI was studied according to the type of progestogen included in third generation (that is, desogestrel or gestodene) and second generation (that is, levonorgestrel) oral contraceptives, the dose of oestrogen, and the presence or absence of prothrombotic mutations. A cohort of 248 women aged between 18–49 years were enrolled, with acute MI between 1990 and 1995, and matched to 925 control women who had not had an acute MI. Subjects supplied information on oral contraceptive use and major cardiovascular risk factors. An analysis for factor V Leiden and the G20210A mutation in the prothrombin gene was conducted in

217 patients and 763 controls. The risk of MI was increased among women who used second generation oral contraceptives, but the risk appeared to be lower with third generation preparations. The risk of myocardial infarction was similar whether or not they had a prothrombotic mutation.

▲ **Tanis BC**, van den Bosch MAAJ, Kemmeren JM, Cats VM, Helmerhorst FM, Algra A, van der Graaf Y, Rosendaal FR. Oral contraceptives and the risk of myocardial infarction. *N Engl J Med* 2001;**345**:1787–93.

## Heart failure

### Valsartan: not an agent for universal use ►

Over 5000 patients with heart failure were randomly assigned to receive 160 mg of valsartan or placebo twice daily. Although overall mortality was similar in the two groups, valsartan significantly reduced the combined end point of mortality and morbidity (defined as the incidence of cardiac arrest with resuscitation, hospitalisation for heart failure, or receipt of intravenous treatment) and improved clinical signs and symptoms in patients with heart failure. However, a post hoc observation of an adverse effect on mortality and morbidity in the subgroup receiving valsartan, an ACE inhibitor, and a  $\beta$  blocker at the same time raises concern about the potential safety of this specific combination.

▲ **Cohn JN**, Tognoni G, for the Valsartan Heart Failure Trial Investigators. A randomized trial of the angiotensin-receptor blocker valsartan in chronic heart failure. *N Engl J Med* 2001;**345**:1667–75.

**Male cells in a female heart ►** Cases in which a male patient receives a heart from a female donor provide an unusual opportunity to test whether primitive cells translocate from the recipient to the graft and whether cells with the phenotypic characteristics of those of the recipient ultimately reside in the donor heart. The Y chromosome can be used to detect migrated undifferentiated cells expressing stem cell antigens and to discriminate between primitive cells derived from the recipient and those derived from the donor. Myocytes, coronary arterioles, and capillaries that had a Y chromosome made up 7–10% of those in the donor hearts and were highly proliferative, suggesting migration of primitive cells from the recipient to the grafted heart.

▲ **Quaini F**, Urbanek K, Beltrami AP, Finato N, Beltrami CA, Nadal-Ginard B, Kajstura J, Leri A, Anversa P. Chimerism of the transplanted heart. *N Engl J Med* 2001;**346**:5–15.

**In vivo detection of apoptosis ►** Cardiomyocyte apoptosis occurs during reperfusion injury, transplant rejection, and heart failure, but detection of apoptosis in the living organism has been limited to histologic analysis of biopsy specimens (TUNEL staining). These two studies describe in vivo techniques for imaging apoptosis in living hearts based on annexin-V binding to externalised phosphatidylserine. Detecting apoptosis in patients would provide valuable information about their clinical condition. It could also be an important window into potential pathogenetic mechanisms. In a study of 18 cardiac transplant patients, five patients showed histologic evidence of transplant rejection (indicated by mononuclear cell infiltration or more severe features) and apoptosis (as revealed by immunohistochemical staining for activated caspase-3). These same five patients were found to exhibit myocardial uptake of the  $^{99m}\text{Tc}$ -annexin-V probe.

▲ **Narula J**, Acio ER, Narula N, Samuels LE, Fyfe B, Wood D, Fitzpatrick JM, Raghunath PN, Tomaszewski JE, Kelly C, Steinmetz N, Green A, Tait JF, Leppo J, Blankenberg FG, Jain D, Strauss HW. Annexin-V imaging for noninvasive detection of cardiac allograft rejection. *Nature Med* 2001;**7**:1347–52.

▲ **Dumont EA**, Reutelingsperger CPM, Smits JFM, Daemen MJAP, Doevendans PAF, Wellens HJJ, Hofstra L. Real-time imaging of apoptotic cell-membrane changes at the single-cell level in the beating murine heart. *Nature Med* 2001;**7**:1352–5.

## General cardiology

**PFO and the risk of stroke** ▶ A patent foramen ovale (PFO) on its own may have a risk of stroke, but how large is the risk? Of 581 patients (aged 18–55 years) who had had an ischaemic stroke of unknown origin within the preceding three months, after four years the risk of recurrent stroke was 2.3% (95% CI 0.3% to 4.3%) among the patients with PFO alone, 15.2% (95% CI 1.8% to 28.6%) among the patients with both PFO and atrial septal aneurysm, and 4.2% (95% CI 1.8% to 6.6%) among the patients with neither of these cardiac abnormalities. There were no recurrences among the patients with an atrial septal aneurysm alone. All were on aspirin 300 mg/day. The presence of both cardiac abnormalities was a significant predictor of an increased risk of recurrent stroke (hazard ratio for the comparison with the absence of these abnormalities 4.17, 95% CI 1.47 to 11.84), whereas isolated PFO, whether small or large, was not.

▲ **Mas J-L**, Arquizan C, Lamy C, Zuber M, Cabanes L, Derumeaux G, Coste J, for the Patent Foramen Ovale and Atrial Septal Aneurysm Study Group. Recurrent cerebrovascular events associated with patent foramen ovale, atrial septal aneurysm, or both. *N Engl J Med* 2001;**345**:1740–6.

### Journals scanned

American Journal of Medicine; American Journal of Physiology: Heart and Circulatory Physiology; Annals of Emergency Medicine; Annals of Thoracic Surgery; Archives of Internal Medicine; BMJ; Chest; European Journal of Cardiothoracic Surgery; Lancet; JAMA; Journal of Clinical Investigation; Journal of Diabetes and its Complications; Journal of Immunology; Journal of Thoracic and Cardiovascular Surgery; Nature Medicine; New England Journal of Medicine; Pharmacoeconomics; Thorax

C Baker, E Barnes, V Bhatia, R Desilva, M Earley, K Fox, D Gorog, G Jenkins, R Kaprilian, A Kapur, M Khan, P Lambiesse, V Markides, M Poullis, P Ramrakha, J Strange, B Wasan, H Walker

## IMAGES IN CARDIOLOGY

**Myocardial viability by contrast enhanced MRI in a patient with left bundle branch block showing a severe defect on FDG-PET**

A 53 year old male hypertensive patient with no history of previous myocardial infarction presented with exertional dyspnoea and fatigue. The ECG revealed complete left bundle branch block (LBBB), and echocardiography demonstrated moderately reduced left ventricular function (ejection fraction 36%) with anteroseptal and anteroapical located severe hypokinesia and akinesia. Assessment of myocardial viability using  $^{18}\text{F}$ -fluoro-deoxyglucose (FDG) positron emission tomography (PET) (left panels showing a midventricular short axis view (top) as well as a horizontal (middle) and a vertical (bottom) long axis view) revealed a severe defect of the septum from base to apex extending to the anterior and inferior wall (white arrowheads) suggesting scar tissue. Contrast enhanced cardiac magnetic resonance imaging (MRI) 15 minutes after gadolinium-DTPA administration using a T1 weighted gradient echo sequence optimised for the detection of scar tissue (which presents as bright myocardial enhancement as opposed to normal black myocardium) revealed complete absence of scar (right panels showing corresponding short axis and long axis views). Atherosclerotic coronary artery disease was excluded at coronary angiography.

The finding of a reduced tracer uptake on FDG-PET images in the septal region of patients with LBBB is not uncommon, leaving uncertainty about the viability status. In this patient with LBBB and severely abnormal FDG-PET scan, absence of scar tissue in the septal region and hence myocardial viability could be confirmed using contrast enhanced MRI. Thus, contrast enhanced MRI may be a valuable adjunct for the assessment of myocardial viability in patients with regional severe wall motion abnormalities and LBBB.

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